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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/483,588	01/14/2000	Leonard Presta	P1726R1	8570

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EXAMINER
SAUNDERS, DAVID A

ART UNIT	PAPER NUMBER
1644	21

DATE MAILED: 04/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
483,588	PRESTA
Examiner	**Group Art Unit**
SAUNDERS	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 12/3/02.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1-2, 4-15, 23-30, 36-37, 50-61 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1-2, 4-6, 8-15, 23-30, 36-37, 50-61 is/are rejected.

☑ Claim(s) 2 is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Action Summary

Part of Paper No. 21

The amendment of 12/3/02 (paper 17) has been entered.

Claims 1-2, 4-15, 23-30, 36-37 and 49-61 are pending and under examination. New claims 50-60, however, are only examined for the elected embodiment of group I- i.e. Variants with increased binding activity to at least one Fc receptor.

Drawings filed on 2/25/03 have been approved by the draftsman.

Claim 6 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 6 fails to limit claim 1 since recitation of "Fc gamma RI" has been incorporated into claim 1.

Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 7 fails to limit claim 1, since claim 1 already requires at least two amino acid substitutions.

Claims 23 and 27 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 23 recites positions 276, 309, 320, 322, 331, and 334, which are not recited in claim 14. In like manner further dependent claim 27 recites positions 276, 309, 320, 322 and 331, which are not recited in claim 14.

Claims 4, 10, and 50-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 depends from cancelled claim 3.

Claim 10 remains indefinite because the term "lower" as a modifier of "hindge region" is a relative term. Applicant has urged that page 16, lines 21-24 define the "lower hindge region ". The examiner finds that the specification merely recites what the art "normally defines" as the "lower hindge region". However, the text does not indicate that applicant's claim terms are limited thereto.

Claim 50 must be amended to recite the elected embodiment of group I.

Claims 50-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 50 and 61 recite new matter.

While the specific residue positions recited in claim 50 are supported, applicant has no support for merely reciting these positions per se, without the requirement that the modification (5) at these positions result in a polypeptide having an altered Fc binding property and/or altered ADCC activity.

New claim 61 contains new matter because it does not stipulate that the more effective ADCC occurs " in the presence of human effector cells", as recited in original claim 1. If applicant has support for not limiting this claim to ADCC in the presence of

human effector cells, applicant must point out the basis for support by specification page and line number.

Applicant's amendment of claim 1 has overcome previously stated prior art rejection, based on Better et al. and Sarmay et al.

The amendment of claims 1 and 14 has only overcome previously stated prior art rejections based upon Chappel et al. with respect to claim 1 and its dependents.

The amendment of claims 1 and 14 has overcome previously stated prior art rejections based upon Morgan et al. and Idusogie et al. for claim 1 and its dependents as well as for claims 14-15. It has not overcome the rejection of claims 23 and 27-28.

Claims 14-15 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Chappel et al. (JBC, 268, 25124, 1993), for reasons of record in paper 14.

Applicant has urged that the cancellation of position 309 in claim 14 has overcome. The examiner fails to see how this overcomes, because in the statement of the rejection the examiner pointed to the substitutions shown by Chappel et al. in Table 2. These show a modification at position 339, as well as at 309.

Also, even if cancellation of position 309 had overcome the rejection of claim 14, it would not have overcome the rejection of dependent claim 23, which still recites "309".

Claims 23 and 27-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Morgan et al. (WO 94/29351), for reasons of record (paper 14).

Applicant considers that the rejection has been overcome due to cancellation of position 320 in claim 14. Since claims 23 and 28 still recite "320", these claims and intervening claim 27 remain rejected.

Claims 23-24 and 26-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Idusogie et al. (6,242,195), for reasons of record.

The amendment canceling recitation of various positions in claim 14 has not overcome, because these positions are still recited in claims 23 and 28.

Applicant's urgings filed on 12/3/02 have been considered but are not convincing.

Upon reconsideration of the claims, a new reference is cited herein below.

Claims 1-2, 4-6, 8-11, 14-15, 23-24, 36, 50, 53 and 59-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Steplewski et al. (PNAS, 85,4852,1988).

Steplewski et al. compare the effects function of four variants of a mouse-human chimeric antibodies directed against tumor cells. These four variants are IgG1, IgG2, IgG3 and IgG4, all of which have a human Fc region, in accord with instant claims,1 and 61. The IgG1 variant shows superior ADCC activity. As previously argued (paper 14) in the rejection over Better et al, it is considered that Fc gamma RIII is critical for mediating ADCC (instant specification pages 27-28). Hence, anticipation of better binding to this receptor, as stated in claims 1 and 61 is considered to be inherent. The IgG1 may be properly considered as a "variant" of any of the other three subclasses IgG2, IgG3, or IgG4; IgG1 differs from each of the other subclasses at "two or more amino acid substitutions" (instant Fig. 22A), as recited in claim 1. Claim 1 is thus anticipated.

Dependent claims 2, 4-6, 8-10 are rejected since their limitations are consistent with what is taught by Steplewski et al. and with what instant Fig.22A shows as the inherent difference between IgG1 and the three other IgG subclasses.

Claim 11 is included because one of the positions at which IgG1 differs from IgG4 is at position 330, which is recited in the Markush group of claim 11. See Fig. 22A.

Claims 14-15 are included because IgG1 differs from IgG2 at positions 296 and 327; because IgG1 differs from IgG3 at positions 296 and 435; and because IgG1 differs from IgG4 at positions 268, 296, 327, 330, 382 and 419.

Claims 23-24 are included because IgG1 differs from IgG4 at positions 268, 330 and 331.

Claim 36 is included because mice were injected with the chimeric antibodies (p.4853, col.1) in what must have inherently been a pharmaceutical carrier.

Claim 50 is included because IgG1 differs from IgG4 at position 330.

Dependent claims 53 and 59-60 are consistent with the teachings of the reference.

Claim 61 is rejected, following the same rational applied to claim 1.

Claims 1 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steplewski et al.

Steplewski et al have been cited supra against claims 1 and 35. Since they suggest use of the IgG1 chimeric antibody for human therapy (p. 4856), sterilization would have been obvious since such is conventional for the protection of patients.

Claims 14-15, 23-28, 50, 53, 55 and 59-60 are rejected under 35 U.S.C. 102(e) as being anticipated by Idusogie et al. (6,528,624).

Idusogie et al. ('624) show mutants in addition to those shown by Idusogie et al. ('195). See Table 3 at col. 42.

Note mutant K326A, corresponding to mutant no. 51 in Instant Table 6; which shows its increased binding t o Fc gamma RIIB.

Note mutant E333A corresponding to mutant no. 54 in instant Table 6 (page 73, row 7), which shows its increased binding to Fc gamma RIIIA and its decreased binding to Fc gamma RIIB.

From the above considerations, claims 14-15, 23 and 50 are anticipated, since claims 14 and 23 and 50 recite 326 and 333.

Claims 24-26 are anticipated by the E333A mutant.

Claims 27-28 are anticipated by the K326 A mutant.

Dependent claims 53, 55 and 59-60 have limitations consistent with the above noted teachings of Idusogie et al.

As noted previously for Idusogie et al. ('195), though the reference did not recognize the characteristics instantly recited, these characteristics were inherent, as shown in instant Table 6.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 14-15, 23-28, 50, 53, 55 and 59-60 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12 and 18 of U.S. Patent No. 6,528,624. Although the conflicting claims are not identical, they are not patentably distinct from each other because as explained, supra the K326A and E333A mutants of Idusogie et al. anticipate the rejected claims. These mutants would be encompassed by issued claims 12 and 18. Since instant and copending claims encompass common subject matter a disclaimer is required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday-Thursday 8 am - 5:30 pm. and on Alternative Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Application/Control Number: 09/483,588

Art Unit: 1621

Saunders/tgd
April 8, 2003

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1649